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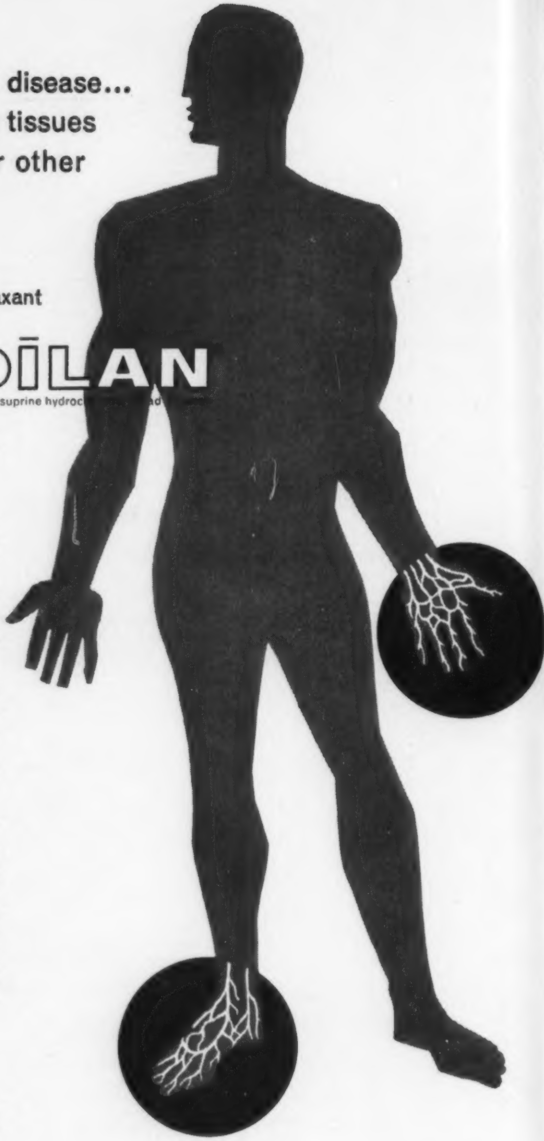

CLINICAL PROCEEDINGS

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The Thymus Problem—No Problem at All

DONALD W. WICZER, M.D.*

For well over 300 years the thymus has been incriminated and as many times exonerated as the cause of symptoms, disease and death in man.[1] In the past 50 years, results of research by numerous investigators on the role of the thymus in health and disease, with particular attention to the thymus as a possible cause of disease in infants and children, have appeared in the literature. The thymus problem as a topic of discussion probably reached its peak in popularity some 20 years ago with pediatricians, surgeons and radiologists being tagged either as "thymus men" or "nonthymus men." The importance of the problem warranted a panel discussion on the thymus gland under the auspices of the American Academy of Pediatrics,[2] at which time conclusions were drawn which included the suggestions that the term "status thymicolymphaticus" be dropped, and that there was no primary relationship between thymic size or position and sudden death. The outcome of the discussion might have been considered a victory for the "nonthymus men" or at least a turning point of the long argument in their favor. The last strong paper in favor of the beliefs of the "thymus men," namely that the thymus gland, in and of itself and by virtue of its size and position, could be the direct and sole cause of sudden death, was written by Carr[3] and published in 1945. A trend de-emphasizing the role of the thymus as an organ of clinical importance in pediatric practice has been present for the past 10 to 20 years. Since the thymus problem has not been completely resolved, and since instances of disease manifested particularly by respiratory symptoms which could possibly be thought to be caused by enlarged or abnormal thymuses continue to appear in infants, it is believed that a general discussion of the thymus problem is warranted.

THE "NORMAL" THYMUS

The thymus in the past has at times been grouped with lymphoid tissue, at times with endocrine tissue, and sometimes with both types of tissue. It is said to arise from the ventral diverticulum of the third (and sometimes the fourth) branchial pouch.[4] The parathyroids are said to arise from the corresponding dorsal diverticulum, and, therefore, frequently one tissue may be found buried in or surrounding the other.[3] The thymus descends from the neck to the thorax during fetal life. In some instances descent may be held up anywhere along the route, leading to the presence of

* Assistant Chief Resident, Children's Hospital.

aberrant thymic tissue. At birth, the thymus is described by various investigators as weighing an average of 10 Gm.,[5] or 13 Gm.,[2, 6, 7] and ranging in weight from 3 to 31 Gm.,[4] 4 to 20 Gm.,[3] and 10 to 14 Gm.[8] It is relatively much larger at birth and in early infancy, losing weight during the first few weeks of life and then increasing in size and weighing as much as 17 Gm. by the sixth week.[7] It is said to be broad in fetuses and elongated or molded in infants who have breathed. The thymus reaches its greatest weight at puberty when it has been reported variously as weighing an average of 32 Gm.,[2] 35 Gm.[6, 8] and 37.5 Gm.[3] The thymus is largest during the period of greatest growth. Involution begins at puberty, and the thymus may weigh 15 Gm. or less during adult life. According to Donaldson,[9] Galen was the first to note that the thymus underwent involution and also that it reached its greatest size at puberty. It may not completely disappear in adult life, and probably the term "persistent thymus" is a misnomer.[6]

According to Currarino and Silverman,[10] great variation exists in the size and shape of the thymus in normal infants. Caffey[11] feels that the limits of normal variation in the size, shape and position of the thymus have not been satisfactorily established. The size of the thymus varies proportionally with the weight of the individual and his state of nutrition. Other factors which cause a change in the size and shape of the thymus will be discussed subsequently. According to Caffey, the thymus normally comes to lie in the superior anterior mediastinum, behind the sternum and in front of the trachea, heart and great vessels. This division of the mediastinum and the placing of the structures which are both normally and abnormally present therein is well described and illustrated by Herlitzka and Gale.[12]

Histologically the thymus is described by Boyd[2] as made up of a medullary portion containing Hassall's corpuscles, a cortex made up of a framework containing predominantly lymphocytes, and a supporting connective tissue stroma; the cortex is thought to make up the major portion in early life. After puberty the greater portion of the thymus is made up of fat and connective tissue. Even in middle age, cell mitoses can be observed in the gland, only hinting that the thymus may be physiologically active as a gland of internal secretion.[6] Numerous references, however, voice the popular contention that the thymus has absolutely no proven function in either the pediatric or the adult age groups in clinical medicine.[2, 3, 7] Nelson[4] feels that the thymus may have no other function save lymphopoietic. Arguments which have been used in the past to prove that the thymus functions as an organ of internal secretion include a possible relationship with the thyroid in exophthalmic goiter, a relationship to Mongolian idiocy, and an influence on calcium and phosphorus

metabolism, growth, osteomalacia and many others.[13] These theories have either fallen into disrepute, or the relationships to the thymus have been explained in another way, casting doubt on the thymus as an endocrine gland.

THE THYMUS AND MYASTHENIA GRAVIS

Certain other relationships are less easily refuted, and in fact many are considered to exist today. One is that between myasthenia gravis and thymoma.[11, 12, 14-16] According to Weingarten and Gordon, [17] thymoma as a term was first introduced by Grandhomme in 1900 and was meant to include any malignant tumor of the thymus gland. As described by Seybold et al.,[15] it is a slowly growing tumor of the thymus which arises from both the epithelial and thymocytic elements of the thymic parenchyma which occur in varying proportions. Typical Hassall's corpuscles are absent in most thymomas. It is said that only 15 per cent of patients with myasthenia gravis have thymomas; yet 75 per cent of patients with thymomas have myasthenia gravis.[12, 14, 15] As yet there is no suitable explanation for this relationship. Benign thymoma (71 per cent of all thymomas are benign, 29 per cent are malignant),[12] has also been associated with agenesis of erythrocytes, 12 instances having been noted since 1928, and two more recently having been reported by Bayrd and Bernatz.[18] Much more has been written concerning thymoma, but further discussion is beyond the scope of this paper.

THE THYMUS AS A LYMPHOPOIETIC ORGAN

The thymocyte is morphologically identical to the mature lymphocyte. A lymphopoietic function of the gland is described by Simmons.[19] He also draws attention to the relationship of thymic function and leukemia and claims the abnormal cells are formed in the thymus and migrate from it. Citing data to support this thesis, he feels a trial of thymectomy in leukemia might be warranted.

THYMIC ENLARGEMENT

Certain changes in size of the thymus which are evidenced by enlargement of the superior mediastinal shadow by x-ray are noted when other clinical conditions are present in man and should be mentioned. Hyperplasia of the thymus is said to be associated with adrenalectomy, thyroidectomy, castration, a state of excellent nutrition, short chunky children living in cool climates, exophthalmic goiter, Addison's disease, acromegaly, congenital hypoplasia of the adrenals, anencephaly, status thymicolymphaticus, and occasionally with myasthenia gravis, rickets and hypophysectomy. Persistence of the thymus in adults has been said to cause tallness,

slenderness, thin texture of skin and hair and low resistance to infections,[13] but it is certain that the thymus is neither a direct nor indirect cause of these latter changes. The thymus shadow is reduced roentgenographically in starvation and inanition, chronic disease, asthenia, warm climate, fever and exhaustion.[3, 11, 20] Irradiation reduces the thymic shadow rapidly, but according to Caffey,[11] the thymus regenerates in a few months after irradiation. The prenatal use of iodized salt is said to reduce the incidence of enlarged thymus,[21] but this is probably via stimulation of thyroid function in goiter areas.

Although thymus size is measured roentgenographically it has been emphasized repeatedly that great error exists in such a procedure. Currarino and Silverman[10] describe the thymus as varying considerably in size and shape and often causing widening of the mediastinum on one or both sides. The thymus may extend downward into the costophrenic angle and completely obscure the cardiac silhouette. The thymic lobes may be globular or sail shaped. The thymic shadow is exaggerated in expiration and the mediastinal shadow narrowed when the heart is pulled downward on inspiration.[10] Caffey[11] states that shadows are larger when the patient is recumbent than when he is x-rayed in the upright position. He feels the commonest cause of spurious diagnosis of thymic hyperplasia may be filming in slight rotation. Flexion of the neck may also change the size and shape of the thymus.[20] It is stated that for all the above-mentioned reasons and more, the mediastinum may look differently in x-rays of the same child taken 10 minutes apart.[16] Donaldson[9] states that one needs fluoroscopy as well as x-ray for positive diagnosis of enlargement of the thymus. Caffey[11] states that, "The thymic shadow is always blended with surrounding structures, and therefore roentgen signs of enlargement or estimation of size and shape is uncertain in film and fluoroscopy as well." He suggests that the signs diagnostic of thymic enlargement are increase in the width of the mediastinal shadow in the frontal plane and increase in depth in the lateral projection. Diagnostic pneumomediastinum has been advocated in questionable cases, but this procedure is seldom used.[10] Since other mediastinal structures may be the cause of the increased size of the shadow, and since standards for normal size of the thymus and its variations are wanting, particularly in neonates and infants, there is uncertainty in diagnosing thymic size by x-ray.

THE THYMUS AND SUDDEN DEATH

With the preceding as background, the next question to be considered is whether or not the enlarged thymus can cause disease and death. Classically, the symptoms attributed to thymic disease have been stridor, cyanosis, wheezing and choking attacks, but many other symptoms have

also been suggested. In the past, five principal theories have been proposed to explain how the thymus produced symptoms and death:[1, 2, 22] 1) the theory that death is due to hypersusceptibility to a physical or chemical agent; 2) the theory of abnormal thymic secretion leading to lymphotoxemia and death; 3) the theory of anaphylaxis with liberation of a nucleoprotein from lymph nodes which either directly or indirectly causes death; 4) the concept of status thymicolymphaticus in which a constitutional defect coupled with hyperplasia of the thymus (especially in the medullary portion) and a generalized lymphoid hyperplasia possibly associated with hypoplasia of the adrenals (with the associated hypoplasia of elements of the cardiovascular system) is believed to be the cause of death; and 5) the obstructive theory in which pressure is supposedly exerted on the trachea, blood vessels and various nerves, particularly the vagus and recurrent laryngeals, by an enlarged or abnormally placed thymus.

The first three theories have been the least popular, and insofar as can be determined, proof has not appeared to date to substantiate disease or death caused by the thymus via these routes. Cases of death thought to be due to adrenal insufficiency associated with thymic hyperplasia, as mentioned in Carr's classic paper,[3] are most likely due to the insufficiency of adrenal hormones alone, with resultant lack of lymphoid cell breakdown by the action of cortisone; this is manifested by hyperplasia of both lymphoid tissue and thymus, the latter being in no way a direct or indirect cause of death. The theory of anaphylaxis has been used to explain many deaths due to allergic reactions, but incriminating the thymus in this situation as the cause is unjustified.

The theory of status thymicolymphaticus has been a much more popular one in years gone by. Intermittent dyspnea, cyanotic attacks, intermittent suffocative spasms, stridor, breath-holding spasms with cyanosis and shock, and collapse from seemingly insignificant causes such as minor surgical procedures and anesthesia have all been considered as part of the picture of status thymicolymphaticus;[2] a hyperplasia of the thymus was frequently found at postmortem examinations in patients thought to have died a "thymic death." Carr[3] differentiates status thymicolymphaticus from status thymicoasthmaticus in which he states the patients appear clinically to have asthma unresponsive to epinephrine and show hyperplasia of lymphoid tissue in the submucosa and peribronchial muscle fibrils of the bronchi and bronchioles. The thymuses of these patients are all said to be enlarged but to a lesser degree than those seen in so-called acute tracheal compression. Carr reports 7 cases of status thymicoasthmaticus. One paper describes thymic asthma as mechanical obstruction leading to inspiratory stridor and suffocation and describes mors thymica as unexpected death occurring during sleep where no obstruction is demonstrable. Cases of

hyperplasia of the thymus where the thymus alone is enlarged have been called status thymicus, whereas the term status thymicolymphaticus has been used when hyperplasia of the lymphoid system as well as the thymus has occurred.[6] Bromer[8] lists the following criteria of status thymicolymphaticus which have been proposed to date: enlargement of the spleen, thymus and lymphatic tissues, as well as follicles of the nasopharynx and at base of the tongue, a decrease in development of the chromaffin system, a familial disposition, a predominance in males, muscle flabbiness, skin pallor, lack of strength and resistance to infection, a tendency to eczema and allergy, a relative lymphocytosis and sudden death. During the period when the theory reached its greatest popularity, thymuses were irradiated as a prophylactic measure in patients with thymic enlargement undergoing anesthesia.

The literature contains much argument both for and against status thymicolymphaticus, but popularity began waning 20 years ago, and the diagnosis is no longer considered a diagnostic possibility by the great majority of physicians today. What were then called enlarged thymuses are now known to be the normal thymuses usually seen in patients dying suddenly and unexpectedly of unknown causes, whereas the smaller thymuses which were previously called normal were usually found in patients who came to autopsy after chronic wasting diseases. In 1939, the American Academy of Pediatrics[2] concluded that the term status thymicolymphaticus should be discarded and that the thymus has no obvious function in clinical medicine. Nelson[4] has stated that the evidence available does not justify incrimination of the thymus as a cause of unexpected death. Wilson[6] described thymic death as an "alibi diagnosis" and quoted the Committee of the Medical Research Council in collaboration with the Pathological Society of Great Britain and Ireland in 1931 as saying that there exists no evidence that so-called status lymphaticus had any existence as a clinical entity. Littleton et al.[1] feel that there is little evidence for the thymus as a cause or influence in disease or sudden death and discard all five theories. They state there is no evidence that so-called status thymicolymphaticus has any existence as a pathological entity. Caffey[11] states that every authentic study has refuted the concept of thymic death and draws a parallel between large healthy thymuses and abundant subcutaneous fat in healthy persons. Rabson[5] quotes Simpson as saying, "Status lymphaticus is not more than a status, and if we admit, however unwillingly, the possibility . . . that such subjects may die more readily than others of a trivial cause, that does not excuse the failure to find that cause." He adds, "We should be no more at liberty to say that a person died of flat feet or a dwarf stature or some other status." He feels we must have a willingness to admit inability to fix the cause of death.

Carr,[3] a strong supporter of the thymus as a cause of symptoms and death, felt the term status thymicolymphaticus was used too freely and should be reserved for specific cases and not for any cases of sudden unexplained deaths in children. He may have been right in stating that such diagnostic abuses have in the main been responsible for the disrepute of the thymic status; certainly, no one can disagree with his plea for orderly necropsy proceedings. It is now felt, however, that these more careful autopsies will not uncover more cases of thymic death, as Carr felt, but will show other tenable etiologies for these unexplained sudden deaths. Spain, Bradess and Greenblatt[23] have suggested that quantitative or qualitative deficiency of gamma globulin may have been the cause of many of these sudden deaths, since the peak age incidence of sudden death occurs between the second and fifth months of life, a time when the infant's ability to produce gamma globulin is lowest, and when most transplacental antibodies have been metabolized. The authors studied 52 consecutive instances of sudden and unexplained deaths in infants, and both postmortem findings and serum globulin levels determined in some children added support to their theory.

The theory of obstruction of the trachea, nerves and vessels as a cause of sudden death has been discussed at length in the literature. Mengel[7] feels that congenital hyperplasia of the thymus is "probably more common than we realize," as suggested by the following symptoms: difficulty in breathing, noisy respirations, cough, choking attacks while nursing, cyanosis, and weakness and retraction of the head; convulsions are seen rarely. Upper respiratory infections often complicate the picture. Mengel further states that tracheal compression can be demonstrated only by bronchoscopy and confirmed by x-ray. In Rabson's case[5] postmortem examination revealed distinct antero-posterior compression and luminal narrowing of the trachea by the thymus. Carr[3] cites 49 cases dying of conditions arising from, or directly associated with, pathological changes in the thymus and lymphatic system and feels that the group offers "indisputable examples" of death from asphyxia following tracheal compression from an enlarged thymus and associated lymphatic hyperplasia. Littleton et al.[1] state, "We still have not disproved the fact that an enlarged or abnormally positioned thymus can cause symptoms or death by tracheal compression, but it would be exceedingly rare." They feel, in addition, that the vessels would be compressed before the trachea. Studies on cadavers, using lipiodol, showed no tracheal compression in various positions, but some vascular compression was noted in several.

The differential diagnosis of tracheal compression by an enlarged thymus should include foreign bodies, respiratory infection, retropharyngeal abscess, neoplasms, nasal obstruction, congenital laryngeal stridor, con-

genital malformations, laryngospasm, pneumonia, atelectasis, asthma, meningeal disturbances and intracranial hemorrhages.[7] Mitchell[2] concluded that the thymus occasionally causes symptoms of compression but that one should look for other causes of symptoms of compression first. Caffey[11] feels that there is great doubt that large thymuses ever cause obstructive dyspnea or cyanosis and agrees that other causes should be sought. Rabson[5] points out in the case which he cites that it was not revealed why the fatality took place when it did and not a week earlier or a day later, assuming that the thymic size would not change in an acute manner. Nor can the reason for sudden death due to tracheal compression by an enlarged thymus at one time and not another be explained. In spite of the fact that the space between the vertebral column and the sternum is small and the tracheal rings do not show true cartilaginous development, many pathologists feel that in infants the thymus is too soft to compress the trachea. It is possible to conclude that the thymus could only rarely cause compression of the trachea, that sudden death due to this compression is practically nonexistent, and that it would be hazardous to attribute death to this cause (since many etiologies of sudden death would remain undiscovered). In the group studied by Spain et al.,[23] infections of the respiratory tract seemed to be the major finding at autopsy, and a fulminating infection may have been the cause of death in a number of these patients. The relationship between this problem and plasma gamma globulin levels has already been mentioned. Many authors have suggested the possibility that infection causing enlargement of lymphatics, particularly mediastinal nodes, is responsible for enlargement of the mediastinal shadow seen by x-ray in many of these cases. No conclusion can be drawn as to whether or not an enlarged thymus can cause symptoms of mild or moderate degree such as stridor, dyspnea and wheezing, by pressing on the trachea or other mediastinal structures. The rare exception arises when one is dealing with a thymoma or when mediastinal masses other than normal hyperplastic thymus exist; here, obviously, when enough doubt exists, a thoracotomy should be done, a definite diagnosis made, and definitive or supportive therapy carried out surgically or roentgenologically as indicated.

SHOULD THE "ENLARGED" THYMUS BE IRRADIATED?

In the past the treatment of choice for enlarged thymuses thought to be the cause of symptoms was irradiation. Both thymic and lymphatic tissues are exquisitely sensitive to irradiation. This practice is still carried on, although not so widely as years ago. Many reports show shrinking of the thymus and relief of symptoms following irradiation; others show relief of symptoms but no shrinking of the thymus; still other authors report shrinking of the mediastinal shadow but no relief of symptoms. It has also been suggested that enlarged mediastinal lymph nodes have

been responsible for the symptoms and that relief is obtained by their shrinking rather than by thymic response to irradiation. Larson[20] feels that lymph nodes are involved in almost all upper respiratory infections and in small infants may compress minute air passageways. He believes that since "there is no evidence to date that such therapy is detrimental and every clinical indication that such treatment is warranted," irradiation of the chest would bring about relief of symptoms through shrinking of these nodes and should be employed. Hence, a popular belief in the past has been that irradiation to the chest is successful in relieving symptoms of dyspnea and stridor regardless of what structures in the mediastinum are affected. Many doctors in the past, therefore, who believed the thymus unrelated to respiratory symptoms nevertheless requested the infants be irradiated because they knew that good results were obtainable in most cases. Nelson[4] states that the instances in which x-ray therapy for enlargement of the thymus is indicated are for practical purposes nonexistent, and that routine x-ray of infants and children preoperatively to rule out enlarged thymuses is rarely practical and not indicated.

In 1955, Clark[24] found that in 15 cases of carcinoma of the thyroid in children 15 years of age or younger all patients had received prior x-ray therapy in infancy and early childhood for benign conditions of the head, neck and thorax. Other authors support the observation that an association exists between irradiation and subsequent development of cancer of the thyroid in late childhood and adolescence.[25] Lattman and others[26] report that almost 20 per cent of all the known cases of children with carcinoma of the thyroid in the United States had irradiation to the thymus or neck for some other disease. Of 10 cases of cancer of the thyroid in children seen in the District of Columbia from 1945 to 1955, three were previously irradiated for a thymic condition. Simpson and Hempelmann[27] also agree that therapeutic irradiation in infants may be an etiological factor in cancer of the thyroid in childhood and adolescence, but point out that the increased risk of each individual child is not great and becomes manifest only when large populations have been treated. Aplastic anemia, leukemia and osteochondromas have also been reported in increasing frequency following irradiation to the thymic area, but the relationship and circumstantial evidence has not been so obvious as with thyroid cancer. Therefore, the lack of evidence that the thymus can cause symptoms or sudden death added to evidence of the dangers of irradiation would indicate that it would probably be best that the practice of irradiation to the thymus be discontinued.

SUMMARY AND CONCLUSIONS

From a review of the literature dealing with the "thymus problem" it may be concluded that no problem exists, that roentgenologic estimation

of thymic size is unreliable, that neither death nor symptoms of any clinical significance are caused by thymic hyperplasia, that these symptoms or deaths are best explained in other ways and are the result of other etiologies, and that thymic irradiation is unwarranted and should not be performed.

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Acute Hematogenous Osteomyelitis: a Report of 36 Cases Seen at Children's Hospital 1950–58

Wellington Hung, M.D.*
Donald F. McGavisk, M.D.†

At Children's Hospital an increasing number of admissions of children with acute hematogenous osteomyelitis has been noted during the past few years in spite of its generally reported decreased incidence since the advent of antibiotics.[1, 2] This increase has also been noted by other authors. Dey[3] reported in 1957 that in the five-year period, 1945 through 1949, there were 67 admissions to the Royal Alexandria Hospital for Children in Sidney, Australia, for acute osteomyelitis, while from 1952 through 1956 there were 150, or more than twice as many cases. Infections which predispose to this disease formerly responded well when treated adequately with antibiotics; in recent years, because of antibiotic resistant bacteria, treatment is becoming more difficult. This increase in the number of cases of acute hematogenous osteomyelitis is probably due to an increase in the number of resistant organisms.

A review of all cases of osteomyelitis hospitalized at Children's Hospital from 1950 through 1958 was undertaken to determine the validity of the impression of increased incidence of this disease. All medical records with a discharge diagnosis of osteomyelitis during the years 1950 through 1958 were reviewed, a total of 88 cases. After exclusion of those cases of osteomyelitis due to direct extension of local infection from overlying tissue and those cases without roentgenological evidence of osteomyelitis, a

* Assistant Chief Resident, Children's Hospital.
† Formerly Resident, Children's Hospital.

total of 36 cases of true hematogenous osteomyelitis remained to form the basis for this study.

INCIDENCE

As seen in table 1, the total number of cases of acute hematogenous osteomyelitis admitted to the hospital showed a sharp increase in 1958, the ratio of number of cases of osteomyelitis to total hospital admissions having remained approximately the same in the preceding four years. Table 2 reveals an approximately equal sex distribution and an equal incidence in the white and Negro races. It is felt that the number of cases is not sufficiently large to bear out the two to one predominance in males commonly stated.[4-6]

Table 3 shows the age distribution of the 36 cases; the greatest incidence

TABLE 1

Annual Incidence of Osteomyelitis, Children's Hospital, 1950–1958, Inclusive

Year	No. of Hospital Admissions	No. of Cases	Ratio
1950		6	
1951	9,786	0	
1952	9,761	2	1:4880
1953	9,456	2	1:4738
1954	9,193	4	1:2298
1955	9,394	4	1:2648
1956	10,239	3	1:3413
1957	11,643	4	1:2910
1958	12,210	11	1:1110

TABLE 2

Distribution of Cases by Sex and Race

Male	19	White	18
Female	17	Negro	18

TABLE 3

Age Distribution

Under 1 year	2
1 year	3
2 years	2
3–4 years	9
5–8 years	10
9–13 years	10

occurred from 5 to 13 years of age. It is noted that in this series only 2 cases occurred in infants. Other authors, notably Green and Shannon,[7] noted a tendency toward a decrease in incidence with an increase in age; 47 of 99 patients they reported were less than 5 years of age. Chapple[4] reported that the disease is seen most frequently between 5 and 14 years of age. Caldwell and Wickstrom[6] recorded the average age of 67 patients as 11 years, while Altemeier and Wadsworth[5] reported that 66 per cent of their 71 patients were less than 10 years of age.

PREDISPOSING FACTORS

Local trauma and antecedent respiratory and skin infections have been found to be predisposing factors in acute hematogenous osteomyelitis;[4, 7-10] in newborns there are often associated skin or umbilical cord infections.[1] Trauma as a predisposing factor in newborns and infants is not so significant as in older children.[11] Pyrah and Pain[9] found a history of trauma within two weeks of the onset of the disease in 78 of 103 cases. Green and Shannon[7] reported that 17 per cent had a history of local injury or minor trauma prior to the onset of osteomyelitis, while a preceding infection, usually respiratory, was noted in 55 per cent of their cases.

In the present series, trauma or antecedent infection were present in 19 cases (table 4). No predisposing cause was found in 14 cases. Three cases were associated with sickle-cell anemia. Several recent papers have reported the association of osteomyelitis due to Salmonella and sickle-cell anemia.[12-16] One of our 3 patients with sickle-cell disease had a complicating Salmonella group B infection of the bone.

CLINICAL PICTURE

The onset of acute hematogenous osteomyelitis may be acute with marked systemic symptoms or may be gradual with the development of pain and disability over a period of several weeks. Initially the pain may be mild or severe, intermittent or constant, generalized or localized. With the passage

TABLE 4

Predisposing Factors in 36 Cases of Osteomyelitis

	No. of Patients	
Trauma		10
Infection		9
Respiratory	7	
Skin	2	
Sickle-cell anemia		3
Unknown		14

of time, the pain usually becomes more severe and better localized. Point tenderness, usually in the metaphyseal region, is an important physical finding in the differential diagnosis. Swelling, redness and increased local temperature are also seen over the affected bone. The joint nearest the involved bone is usually held in a position of slight flexion because of protective muscle spasm. Flexion of the joint may be permitted, but extension of the joint is always painful and resisted. It is not uncommon for an effusion to develop in the neighboring joint. A secondary septic arthritis may also develop.

TABLE 5

Temperature on Admission

Temperature (Rectal)	No. of Patients
98.6– 99.8 F	6
100.0–100.8	7
101.0–101.8	8
102.0–102.8	3
103.0 and above	12

TABLE 6

Initial Symptoms in 36 Patients with Osteomyelitis

	No. of Patients
Pain	23
Local swelling	11
Fever	5
Fever and chills	2
Drainage of purulent material	3
Loss of function	1

TABLE 7

Physical Findings on Admission in 36 Patients with Osteomyelitis

	No. of Patients
Local tenderness	34
Fever	30
Local swelling	27
Limitation of joint motion	21
Local heat	20
Local erythema	8
Purulent discharge	3
Joint effusion	3

Table 5 shows the temperature recorded on admission in the present series. Previous administration of antipyretics is not taken into account. This series reiterates that normal or low-grade fever is not unusual in acute osteomyelitis.

Tables 6 and 7 demonstrate the most common symptoms and physical findings in this series. Pain was the most common presenting symptom and local swelling the next most common in our 36 patients. Tenderness over the involved bone was present in 34. Fever was present in 30 patients, and local swelling in 27. Green et al.,[17] and Dickson[18] have emphasized that localized tenderness is the most significant early clinical finding and indicates that the periosteum has been involved.

BONES INVOLVED

As in most other series,[2, 5-7, 17, 19] the femur and the tibia were the most frequent sites of bony involvement (table 8). Multiple bone involvement in acute hematogenous osteomyelitis is not uncommon. There were 2 such cases in our series; one of these patients had osteomyelitis of the metacarpals and metatarsals, and the other involvement of the humerus, radius, ulna and fibula.

LABORATORY FINDINGS

Acute hematogenous osteomyelitis is usually accompanied by a leukocytosis (table 9), but a normal white blood cell count or minimal leukocytosis in the presence of acute osteomyelitis is not unusual.[2, 17] Early in the disease there is no alteration of the red blood cell count, but anemia develops as the disease progresses. The sedimentation rate becomes elevated rapidly, and Peltier[8] states that this is the best guide to the activity of infection.

TABLE 8

Bones Involved

	No. of Patients	
Femur		12
Tibia		12
Humerus		4
Fibula		4
Radius		1
Ulna		1
Ilium		1
Metacarpals and metatarsals		1
Mandible		1
Multiple bones involved		2
Metacarpals and metatarsals	1	
Humerus, fibula, radius and ulna	1	

TABLE 9

White Blood Cell Count on Admission (in thousands)

	No. of Patients
4– 5	2
6– 9	6
10–14	12
15–19	9
20–29	6
30–35	1

TABLE 10

Bacteriology

	No. of Patients	
Positive Blood Culture	9	
Staphylococcus aureus		8
Hemophilus influenza		1
Pus aspirated at surgery	3	
Staphylococcus aureus		2
Pseudomonas aeruginosa		1
Needle Aspiration	3	
Diplococcus pneumoniae		1
Salmonella group B and *Staphylococcus aureus*		1
Pseudomonas aeruginosa		1
All cultures negative	16	
No cultures taken	7	

The causative organism in the majority of cases of acute hematogenous osteomyelitis in children is the *Staphylococcus aureus*. Many authors[4, 7, 8, 18, 20] have reported that the streptococcus is the most frequent causative organism in children under the age of 2 years, while others[17, 21-24] have found as high an incidence of infection with *Staphylococcus aureus* infection in infants as in older children. The reported higher incidence of streptococcus in very young children has been explained by Green and Shannon[7] on the basis of a higher incidence of antecedent upper respiratory infection and relatively less natural immunity to the streptococcus as compared with the staphylococcus in this age group.

Kessel[25] has stated that in acute hematogenous osteomyelitis a positive blood culture can be obtained in approximately 50 per cent of cases, provided that no antibiotic treatment has been given prior to taking the culture. In this series, bacteriological diagnoses were established by three methods:

1) blood culture, 2) culture of draining lesions, and 3) needle aspiration. Of the 25 patients in whom blood cultures were obtained 16 were negative; however, cultures from the lesions, when taken, were all bacteriologically positive (table 10).

DIFFERENTIAL DIAGNOSIS

In 25 of our 36 cases, the diagnosis of osteomyelitis was entertained on admission (table 11). Peltier[8] and Green et al.[17] have reported that a diagnosis of rheumatic fever is made on admission to the hospital in a high percentage of cases of acute hematogenous osteomyelitis, and Lewis and Scheman[26] state that acute rheumatic fever is the commonest condition for which acute hematogenous osteomyelitis is mistaken. In this series, rheumatic fever was considered in the differential diagnosis of 6 patients. In addition to those diseases shown, the differential diagnosis also should include sickle-cell anemia crisis, poliomyelitis, scurvy, tuberculous arthritis, cellulitis, transient synovitis of the hip joint, Ewing's sarcoma, septic arthritis, septicemia, leukemia, and fractures and other traumatic injuries.

In children, any acute illness characterized by a sudden onset, high temperature, pain over a bone in the vicinity of a joint and a high leukocyte count should strongly suggest acute osteomyelitis, and a careful examination for local tenderness over a bone should be carried out.

TREATMENT

With the advent of antibiotics, the treatment of acute hematogenous osteomyelitis has changed from a surgical approach to a medical one. Medical therapy is concerned essentially with specific chemotherapy aimed at destroying the causative organism and with supportive measures to correct dehydration and toxemia.

A search for the causative organism should be made. Reliance must be

TABLE 11

Diagnoses Entertained on Admission in 36 Cases of Osteomyelitis

Diagnosis	No. of Cases in Whom Considered
Osteomyelitis or possible osteomyelitis	21
Possible rheumatic fever and/or osteomyelitis	4
Possible rheumatic fever	2
Cellulitis	4
Septic arthritis	2
Fever of undetermined origin	1
Septicemia	1
Synovitis	1

placed on blood cultures for the bacteriological diagnosis in most patients since the organism is rarely obtained directly from the site of infection. However, cultures may also be taken from material obtained by aspiration or incision of soft tissue or bony abscesses; this should always be done when possible. Additional information may be obtained from cultures of the nasopharynx, throat or skin lesions. It is extremely important to obtain specimens for bacteriologic study before treatment is begun in order that the sensitivity of the organism to antibiotic drugs can be determined.

The best results in treatment of acute hematogenous osteomyelitis are obtained in those patients in whom treatment is started during the first two to three days of the disease. Beerman[27] has recommended that treatment should be started even when the diagnosis is in doubt, and Green et al.[17] feel that therapy should be withheld no longer than 24 hours while bacteriologic studies are in process.

Table 12 shows the methods of therapy used in this series. The antibiotics and their dosage were so variable that no conclusion can be drawn in terms of adequate dosage of antibiotic or the antibiotics of choice. All 36 patients received penicillin intramuscularly while 32 patients also received one or more broad-spectrum antibiotics or sulfonamides. Surgery included only sequestrectomy, saucerization and osteotomy.

At this hospital we are now using crystalline penicillin G in aqueous suspension given intravenously in a dosage of one million units every three hours until sensitivity studies are available. If the causative organism is sensitive to penicillin, intravenous therapy is continued for a total period of one to two weeks, depending on the severity of the osteomyelitis. Following intravenous therapy, procaine penicillin is given intramuscularly for an additional two to three weeks, the total length of therapy depending on the clinical response. If the causative organism is resistant to penicillin, massive doses of the appropriate antibiotic or antibiotics are given intravenously for approximately two weeks; intramuscular administration of the drug is given for an additional two to three weeks. Oral administration of the appropriate antibiotic may be continued for another one to two weeks, depending on the clinical response. In those patients in whom the

TABLE 12
Treatment

	No. of Patients
Chemotherapy alone	29
Chemotherapy and surgery	7

TABLE 13

Results Following Treatment in 36 Patients with Osteomyelitis

	No. of Patients	
No complications		17
Complications		8
Chronic osteomyelitis	5	
Pathological fracture	1	
Growth disturbance	2	
Still being followed		5
No follow-up available		5
Deaths		1

causative organism is not isolated, changes in the initial antibiotic treatment are dependent upon the clinical response.

Surgery should be held to an absolute minimum and used only for the purpose of drainage in the acute phase.[26, 28] Surgery is reserved mainly for the treatment of chronic osteomyelitis.[8] Dey[3] stated in 1957 that with the increased number of organisms resistant to antibiotics, surgery will play a more important role in the treatment of acute hematogenous osteomyelitis.

COMPLICATIONS

The important complications and sequelae of acute hematogenous osteomyelitis include septic arthritis, pathologic fractures, dislocations, growth disturbances and chronic osteomyelitis. Table 13 shows the incidence of complications in 36 patients, all of whom received treatment. The one death in this series was in a 3 year old white girl who had leukemia and had been treated with aminopterin for the three months prior to her death. The diagnosis of osteomyelitis was substantiated at autopsy. Complications in this series included chronic osteomyelitis, pathological fracture and growth disturbances in the involved extremity.

SUMMARY

A series of 36 infants and children with acute hematogenous osteomyelitis admitted to Children's Hospital from 1950 to 1958 is presented. The recent increase in yearly number of cases of acute hematogenous osteomyelitis observed in this and other series is probably due to an increase in the number of resistant organisms.

In children, any acute illness characterized by a sudden onset, high temperature, pain and local tenderness over a bone in the vicinity of a joint, and a high leukocyte count should strongly suggest acute hematogenous osteomyelitis.

Staphylococcus aureus was the most frequent causative organism in children in this series. Reliance on blood cultures and sensitivity studies is stressed.

Early vigorous treatment in acute hematogenous osteomyelitis is of the utmost importance in order to prevent one or more complications.

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Duplication of the Stomach and Duodenum Associated with Congenital Heart Disease: a Case Report

George C. Emmanouilides, M.D.*

Duplications of the alimentary tract are considered to be rare congenital anomalies. The true incidence of these anomalies is difficult to ascertain because of the relatively wide variation in the symptoms and signs which they may cause. In many instances the symptoms and signs are not evident until adult life. The rarity of these anomalies is evidenced by the report of only 25 cases in a 21 year period from the surgical service of a children's hospital.[1] Duplications of the stomach are much more infrequent than of other parts of the alimentary tract. In a series of 67 cases of duplication of the alimentary tract reported from another children's hospital, the stomach was involved in only 2 cases.[2] In a recent review of the English literature, Kiesewetter[3] found 27 cases of duplication of the stomach and added one more case of his own.[4-26] Since then, two more reports have appeared, adding 3 more cases to the total number reported.[27, 28] Of the 31 reported cases, 19 occurred in the pediatric age group. In this report we present one more case encountered in an infant who came to autopsy at this hospital; in this infant there was, in addition, an associated congenital heart disease.

CASE REPORT

An 8 week old Negro boy was admitted to Children's Hospital February 16, 1959 because of respiratory difficulty present soon after birth. He was born normally after an 8 month gestation. There were no complications during the pregnancy. The birth weight was 6 pounds 8 ounces. The infant was discharged from the hospital at the age of 4 days, and the parents were told that the baby was "healthy." Soon after discharge, however, the mother noticed that the baby breathed rapidly. He took his feedings fairly well although he occasionally vomited some of them. The "shortness

* Research Fellow in Hematology; formerly resident in pathology, Children's Hospital.

of breath" was aggravated when the child was in the supine position and while asleep. There was less respiratory difficulty after taking his feedings and being held, but he became fatigued easily. No cyanosis was noted. Six days prior to admission he was examined by a physician who heard a "blowing systolic murmur" and advised hospitalization. The infant had gained 2 pounds over the birth weight up to that time.

The mother was 33 years old and had leucoderma. She had been treated with penicillin for syphilis during her second pregnancy which ended normally in a healthy child. Three years previously she had had a miscarriage (by a previous husband). Three older siblings had been hospitalized in this hospital because of intermittent abdominal pain and distention. No etiology was found after a thorough study including x-ray examination of the gastrointestinal tract.

Physical examination on admission to the hospital disclosed a thin, well developed, irritable infant, who was afebrile but who was breathing rapidly (60 per minute) with some substernal retraction. There was no cyanosis. The lungs were clear to percussion and auscultation. A grade III high-pitched blowing systolic murmur was heard over the precordium. The liver was palpable 2.5 cm. below the costal margin. No palpable abdominal masses were elicited. There was a left inguinal hernia. The remaining physical examination was not remarkable. The blood count and the urinalysis were within normal limits. A chest x-ray revealed the cardiac silhouette to be abnormal in contour and to occupy a large portion of the left chest. There was an increase in the bronchovascular markings of the lungs. The electrocardiogram was interpreted as showing evidence of biventricular hypertrophy and diffuse myocardial ischemia.

During hospitalization his general condition remained unimproved. On one occasion he developed a temperature of 102° F. He took his feedings very poorly and did not gain weight. His pulse rate varied between 130 and 180 per minute. On the thirteenth hospital day he developed severe respiratory distress with slight cyanosis. His heart rate was 188 per minute. The liver was palpable 4.5 cm. below the costal margin. He was digitalized immediately and placed in an oxygen tent. In spite of the above measures, he expired on the same day at the age of 61 days.

AUTOPSY FINDINGS

The pertinent autopsy findings were as follows: The heart was twice the normal weight, and there was hypertrophy of the myocardium of both ventricles. A small interauricular septal defect measuring 1.0 x 0.2 cm. and a high ventricular septal defect measuring 1.0 x 0.5 cm. were present. There was no evidence of subendocardial fibroelastosis. The lungs showed marked congestion of the vessels and partial atelectasis. The esophagus was empty, and the mucosa was not remarkable. The stomach contained a very small amount of grayish mucoid substance, and the mucosa showed diminished rugal pattern. On the greater curvature, 2.0 cm. distal to the cardiac orifice, there was a large cystic structure measuring 5.5 x 3.5 x 3.0 cm. which was incorporated within the gastric wall (fig. 1). A similar smaller cyst measuring 2.4 x 2.0 x 1.2 cm. was present on the same curvature at the pyloric level. On section, the cysts contained 28 ml. and 8 ml. respectively of cloudy mucoid fluid. The lining mucosa was slightly irregular and had a few dark red punctate discolored areas. There was no communication with the gastric cavity. The lateral wall of the larger cyst was considerably thinner in comparison to the wall of the smaller cyst. A movable 3.0 cm. spherical, dark brown cyst was present in the left duodenal wall and covered the anterior surface of the pancreas. It contained 8.0 ml. of dark brown liquid. No com-

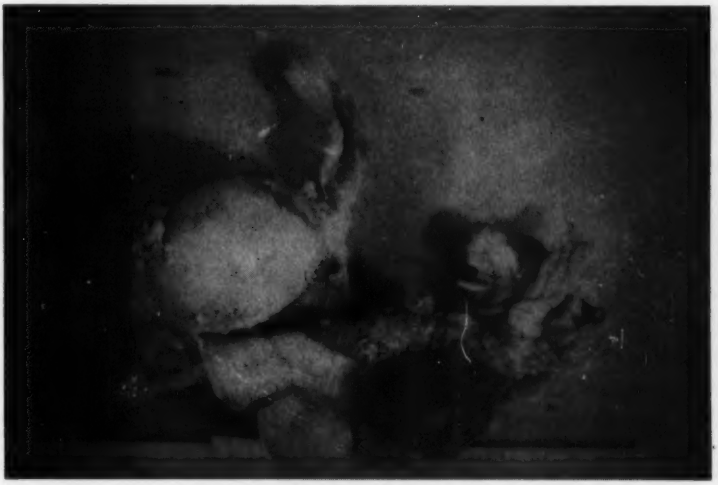

FIG. 1. Posterior view of the stomach and pancreas. The large cystic dilatation overlies the fundus at the level of the greater curvature. The smaller one, inferior to the pancreas is at the level of the pylorus. The dark cystic structure is a duplication lying outside and adjacent to the pancreas.

munication could be found between the cyst and the duodenum, bile ducts or pancreatic ducts. The remaining bowel was not remarkable.

The large cyst was found to be lined with a single layer of columnar epithelial cells when examined microscopically. The submucosa was made up of loosely arranged connective tissue which was overlaid by a layer of smooth muscle. The smaller cyst of the pylorus showed the muscular wall to be contiguous with the wall of the stomach. The lining of this cyst was composed of a relatively normal gastric mucosa except for a compressed portion where the glandular structure was no longer present and where the mucosal surface was made up of flattened columnar epithelial cells. The wall of the duodenal cyst was adjacent to the pancreas and duodenum and was made up of connective tissue. The lining cells were no longer identifiable, but collections of brown pigment which did not stain for iron were present on the surface and in the superficial portion of the tissue.

DISCUSSION

Duplications of the alimentary tract are spherical or elongated hollow structures which possess a coat of smooth muscle, are lined by a mucous membrane similar to some part of the gastrointestinal tract, and are intimately attached to the tract.[2] They may appear at any level from the base of the tongue to the anus but are more commonly found in relation to the small intestine than to any other part of the gastrointestinal tract. The cystic structure may or may not communicate with the lumen of the nearby

alimentary tube. Only two reported gastric duplications have had such a communication.[7, 10] A feature common to all duplications, regardless of size, origin, or attachment, is the possession of a well developed coat of smooth muscle, which may consist of one, two, or three layers. This characteristic differentiates the anomaly from lymphatic or chylous cysts which have considerably thinner walls.

The epithelium which lines a duplication does not necessarily correspond to the normal mucosa of the level at which the duplication is found. The lining may be well preserved, but in some specimens is partially destroyed by pressure necrosis or by enzymatic digestion from the fluid which the structure contains. Commonly the fluid within the duplication is a clear, colorless mucoid substance which has been secreted by its epithelial cells. Sometimes this fluid may be under such high pressure that it results in necrosis and sloughing of the lining membrane. It may then become hemorrhagic.

Duplications may vary greatly in other parts of the alimentary tract. Their secretions produce ulceration in either the duplication or the adjacent intestine, with subsequent gastrointestinal bleeding. This does not occur in duplications of the stomach because of the normal resistance of gastric mucosa to gastric secretions.[3]

EMBRYOLOGY

Bremer[29] has pointed out that the early development of the alimentary tube after the normal stage of solid cord can give rise to hollow structures which do or do not communicate with the alimentary tract. During the late stage of the solid phase, multiple vacuoles appear within the cell mass. These are arranged in linear fashion, and later coalesce and intercommunicate so that a single hollow tube is formed. It is probable that some of these cystic spaces can fail to join the main epithelium-lined tube. This isolated unit could thereby form a hollow duplication (rounded or tubular) which has in its wall all of the histologic elements of some part of the alimentary tract. Sequestration or a pinching off of a group of cells from the primordial intestinal tube could easily account for the development of nearby cysts which contain all the histological elements of an alimentary tract wall and are attached to the intestine or hang from a separate mesentery.[2] Bremer also feels that duplications of the stomach may well occur from an in-pouching of the mucous membrane of the opposite sides, taking an hour-glass form. The mucosal edges become sealed and share a common basement membrane. Following this, the muscular coats proliferate beneath each layer of mucosa, and eventually two separate tubes, attached to each other by a common seromuscular wall, result.

CLINICAL FEATURES

The symptoms and signs which may arise in individuals with duplication of the stomach may center around one or both of two findings. The palpation of a mass in the epigastrium is the commonest finding which leads to investigation. In our case no mass was felt; this was probably due to the fact that the large cyst was located close to the cardia on the fundus of the stomach. Other gastrointestinal symptoms such as vomiting, or signs of partial obstruction, when accompanied by associated positive physical and radiological findings, may disclose a duplication as the cause of the obstruction. Roentgen studies may aid in revealing the size and position of the lesion with relation to other abdominal viscera. A gastrointestinal series may indicate the mass to be behind or below the stomach, and represented by a smooth bulge into the gastric lumen along the greater curvature. In many cases the diagnosis is made during surgical exploration or at autopsy. In a recent report, an 18 day old infant was operated upon because of a suspected pyloric stenosis, which was instead found to be an intramural duplication of the pylorus.[27] Although in our case the clinical picture was dominated by the coexisting congenital heart disease, there is evidence retrospectively that some symptoms may have been the result of the presence of the duplications. The postprandial respiratory distress which the infant presented when placed in his crib and the relief which followed while he was being held indicate that probably the large cyst of the fundus was exerting pressure on the diaphragm, thus further compromising the already impaired cardiac function.

The main objective in the treatment of gastric duplication is to remove as much of the duplication as is technically possible without sacrificing the integrity of the gastric function. The case which is reported here represents a combination of congenital anomalies and emphasizes again the fact that when congenital malformations occur in one system or organ, involvement of other systems or organs may be present and must be suspected. Of the 31 previously recorded cases of duplication of the stomach, none was associated with congenital heart disease.

SUMMARY

In the English literature a total of 31 cases of duplication of the stomach have been recorded through 1958. Nineteen of these were encountered in the pediatric age group. An additional case found at autopsy in a child 2 months old and associated with congenital heart disease is reported. It is of interest that this is the only recorded case of gastric duplication associated with congenital heart disease.

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The Editor's Column

THE PEDIATRICIAN'S ROLE IN SPEECH AND HEARING DEFECTS

Pediatricians and family physicians are often asked to render a judgment on the adequacy of a child's speech or hearing. Parents are expressing concern regarding these aspects of a child's performance at younger and younger age levels. The pediatrician may be able to separate the normal from the non-normal, but evaluation of the non-normal usually calls for the equipment and skills of the specialist in this particular field.

Concern regarding a child's hearing is usually expressed at an earlier age than is concern regarding speech problems. The Ewings, in England, have made exhaustive studies of how normal infants respond to sound, and have provided us with screening tests for evaluating the hearing of infants and very young children. They have found, for example, that infants with normal hearing will automatically localize sound by turning to look in the direction of soft personalized sounds that are of interest to them, but will tend to ignore sounds that are loud or distant or uninteresting. Under the age of 15 months, the test sound should be made on a level with the ear and in a direct line to it, not behind or above the head.

Screening tests, of course, serve only to separate children with grossly normal hearing from those requiring more specific diagnostic testing. Infants who fail to pass the screening tests should be referred to a clinic which has both the equipment and the specially trained staff to conduct more detailed diagnostic tests. Children, 5 years of age and over, can often be tested in the office of an otolaryngologist whose equipment includes a pure tone audiometer.

Problems of reduced or inadequate speech performance are often found in association with hearing impairment. In response to inquiries as to when the physician should refer for specialized consultation we have usually advised that the child who is not talking by the age of 18 months be referred

for a hearing test. If his hearing is found to be normal, concern about the child's lack of speech need not become serious until about the age of 3 years. At any age, however, when the parents raise a question about their child's hearing and the physician cannot state definitely that normal hearing is present, the child should have a hearing examination.

Problems of speech other than those related to impaired hearing include faulty articulation; this involves the substitution, omission, or distortion of individual speech sounds, as well as voice disorders, stuttering, and cleft palate speech. These problems may be relatively simple or may be so serious as to render the child's speech virtually unintelligible. A child with such severely defective speech usually requires the services of a professional speech therapist. In borderline cases where the speech might be expected to improve without professional help, the decision to refer or to wait should be made in the light of such factors as the child's awareness of his speech deviation and his emotional reaction to it and the degree to which the speech appears unattractive to the listener, as well as an estimate of the time that will be required for the unassisted improvement to take place and the degree of emotional, social and educational difficulty the child may be forced to endure while waiting for his speech problem to "take care of itself."

A child who has failed to develop any speech by the age of 3 years generally requires exhaustive diagnostic tests to disclose the cause of the speech failure, whether it be mental deficiency, hearing impairment, emotional disturbance, or actual organic language disability. A period of diagnostic teaching is often required before a definite evaluation of the problem can be made and appropriate therapeutic and remedial plans can be formulated. The best years for learning to talk are the early years; if one must risk erring in making a referral to the speech specialist, it is far better to err on the side of referring too early rather than to wait until the child has learned to get along without the ability to communicate through speech and has built up all of the emotional and personality problems that this implies.

M. J. F.
E. K. M.
A. L. R.

Book Review

Neurology of Infancy. By ANATOLE DEKABAN, M.D., Ph.D., 406 pages with 185 figures, Baltimore; The Williams and Wilkins Company, 1959, $12.00.

In this new book, the author's stated purpose is to "provide. . . . anatomical and developmental landmarks of the maturation of the central nervous system during the first two years of life," and to "outline the principles of pathology, pathogenesis, and clinical manifestation of neurological disorders occurring during infancy with special emphasis on the differences in nosology between the mature patients and infants. . . . "

In a book of only 406 pages, it is only natural that each of the many sections is quite condensed. Its greatest use might be for the medical student or physician casually interested in the conditions described; the book should not be considered a reference work. One would guess that the author's prime interest and experience are in neuropathology since these sections are relatively completely covered and the photographs of both gross specimens and microscopic slides are uniformly excellent.

The book's first chapter deals with the developmental anatomy and physiology of the nervous system from birth to 2 years; chapter 2 discusses the examination of the infant's nervous system. Following these two introductory sections, the book settles down into a description of the various pathologic states. Presentation varies; in the section on birth injury, the book would have benefited if an obstetrical viewpoint had been presented. The section on vascular disorders is probably one of the book's more adequate. One would have wished the chapters on epilepsy and mental retardation, two disorders of major interest, were more complete in their approach. The chapter on cerebral palsy, while covered adequately from the anatomical point of view, would have benefited from a more detailed description of the clinical manifestations. Other chapters are variable in their amount of over-all material presented and probably could have been improved had the author presented more of controversial points of view. Sections on treatment in general are quite short.

The author adds to the reader's difficulty by not always revealing his reference source; further reading is thus complicated. In addition, references are presented alphabetically at the end of each chapter rather than at the end of each subdivision. The book also suffers from more than its share of proofreading errors.

J. WILLIAM OBERMAN, M.D.

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